

REMARKS

Prior to entry of the instant Amendment, claims 1-50 and 111-117 were pending, with claims 13-48, 50 and 111-117 withdrawn from consideration. Claims 3, 4 and 7 have been cancelled and claims 1, 2, 5, 9, 12, 49 and 111 have been amended. New claim 118 has been added. Therefore, claims 1-2, 5-6, 8-50 and 111-118 will be pending upon entry of the present amendment, with claims 13-48, 50 and 111-117 withdrawn from consideration.

Claim 1 has been amended to specify that the claimed molecular masses are in units of Daltons. Claim 1 has also been amended to specify that the acrylamide co-monomer and the hydrophilic co-monomer are different. Support for this amendment can be found at least, for example, in original claim 4. Claim 1 has been further amended to specify that the co-polymer is "suitable for implantation in a patient." Support for this amendment can be found at least, for example, in the abstract of the specification, which states that the present invention is drawn to "[a] bio-synthetic matrix comprising a hydrogel which is formed by cross-linking a synthetic polymer and a bio-polymer..." together with paragraph [0126] which states that "the bio-synthetic matrix can be used for implantation into a patient...".

Claim 2 has been amended to specify that Y is absent, as well as to remove -NR₄R₅ from the definition of R₁₀.

Claim 5 has been amended to be dependent on claim 2.

Claim 9 has been amended to delete various species of N,N-dialkyl substituted acrylamides from the listing of hydrophilic co-monomers.

Claim 12 has been amended to depend on claim 2.

Claim 49 has been amended to recite the synthesis process of claim 43. Support for this amendment can be found at least, for example, in original claim 43. Claim 49 has also been amended to specify that the acrylamide co-monomer and the hydrophilic co-monomer are different, and to specify that the co-polymer is "suitable for implantation in a patient." Support for this amendment can be found at least, for example, in original claim 4, as well as in the abstract and at paragraph [0126] as described above.

Claim 111 has been amended to be dependent on claim 2.

Claim 118 has been added, and is drawn to the synthetic co-polymer of claim 1, which is suitable for corneal implantation in a patient.

The foregoing claim amendments have been made solely for the purpose of expediting prosecution of the present application and should in no way be construed as acquiescence to any of the Examiner's rejections in this or in any other Office Action issued in the present application. Accordingly, *no new matter has been added*. Applicants reserve the right to pursue the subject matter of the present claims prior to being amended herein in this application or in another related application.

In view of the foregoing claim amendments and the arguments set forth below, Applicants respectfully submit that the claims are now in condition for allowance.

(A) Request for Rejoinder of Claims 13-48, 50 and 111-117

The instant claims possess a common technical feature, *i.e.*, "[a] synthetic co-polymer comprising one or more N-alkyl or N,N-dialkyl substituted acrylamide co-monomer, one or more hydrophilic co-monomer and one or more acryl- or methacryl- carboxylic acid co-monomer derivatised to contain a pendant cross-linkable moiety, said synthetic co-polymer having a number average molecular mass between about 2,000 and about 1,000,000 Daltons, wherein said synthetic co-polymer is reactive with primary amines via the pendant cross-linkable moiety, wherein said one or more N-alkyl or N,N-dialkyl substituted acrylamide co-monomer and said one or more hydrophilic co-monomer are different, and wherein said co-polymer is suitable for implantation." Applicants take the position that this technical feature is not known in the art. Specifically, United States Patent No. 4,614,701 (the '701 patent) does not teach a synthetic co-polymer that is suitable for implantation. Accordingly, Applicants submit that the claims are unified by a common technical feature and satisfy the unity of invention criteria set forth in PCT Rule 13. For at least the foregoing reasons, Applicants respectfully request rejoinder and substantive examination of each of claims 13-48, 50 and 111-117.

(B) Rejection of Claims 1 and 5 under 35 USC §112, second paragraph

Claim 1 stands rejected under 35 USC §112, second paragraph, as allegedly being indefinite. Applicants respectfully disagree. However, solely to expedite prosecution, claim 1 has been amended to specify that the units of molecular mass are Daltons.

Claim 5 stands rejected under 35 USC §112, second paragraph, on the grounds that the limitation "alkyl or lower alkyl" allegedly lacks antecedent basis. Applicants note that claim 5

has been amended to be dependent on claim 2. As such, the limitation “alkyl or lower alkyl” has antecedent basis in claim 2.

(C) Rejection of Claims 1-3, 5, 8-11 and 49 under USC §102(b)

Claims 1-3, 5, 8-11 and 49 stand rejected under USC §102(b) as allegedly being anticipated by Uludag *et al.* (J. Appl. Polym. Sci., 75: 583-592 (2000)). Applicants respectfully disagree. However, solely to expedite prosecution, claim 1 has been amended to specify that the acrylamide co-monomer and the hydrophilic co-monomer *are different*. Furthermore, the co-polymer of claim 1 further comprises an acryl or methacryl carboxylic acid co-monomer “derivatised to contain a pendant cross-linkable moiety, said synthetic co-polymer having a number average molecular mass between about 2,000 and about 1,000,000 Daltons, wherein said synthetic co-polymer is reactive with primary amines via the pendant cross-linkable moiety.” Accordingly, claim 1 is drawn to a synthetic co-polymer comprising three unique co-monomer components, *i.e.*, a terpolymer. In contrast, the polymers of Uludag *et al.* contain only one or two co-monomer components. As such, the Uludag reference does not anticipate claim 1, or claims depending therefrom.

Claims 1-3, 5, 8-11 and 49 also stand rejected under USC §102(b) as allegedly being anticipated by Percot *et al.* (Polymer 41 (2000) 7231-7239). Applicants respectfully disagree. As described above, claim 1 as amended is drawn to a synthetic co-polymer comprising three unique co-monomer components (*i.e.*, a terpolymer). In contrast, the polymer taught by Percot *et al.* consists of only two co-monomer components. As such, the Percot reference does not anticipate claim 1, or claims depending therefrom. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

(D) Rejection of Claims 1-12 and 49 under USC §103(a)

Claims 1-12 and 49 stand rejected under USC §103(a) as allegedly being unpatentable over Elaissari *et al.* (US 7,060,804 B2). Elaisarri *et al.* teaches a method for isolating proteins by employing magnetic colloidal particles made up of *i*) a core with a polymer coating, and *ii*) an envelope comprising a polymer. The Examiner states that the polymer(s) of the core and polymer(s) of the envelope may react to form a co-polymeric species comprising NiPAAm, acrylic acid and N-acryloyxsuccinimide. The Examiner alleges that the instant claims

encompass this species, and further alleges that the claimed polymers may be derived from the teachings of Elaissari *et al.* by routine optimization. Applicants respectfully disagree.

As amended, claim 1 is drawn to "[a] synthetic co-polymer comprising one or more N-alkyl or N,N-dialkyl substituted acrylamide co-monomer, one or more hydrophilic co-monomer and one or more acryl- or methacryl- carboxylic acid co-monomer...wherein said acrylamide co-monomer and said hydrophilic co-monomer are different, and wherein said co-polymer is suitable for implantation in a patient." In contrast, the Elaissari reference does not teach a co-polymer comprising said constituent co-monomers, let alone a co-polymer that is suitable for implantation in a patient. The instant application discloses properties, and methods for determining said properties, associated with co-polymers that are suitable for implantation in a patient (see, *e.g.*, Examples 6-8, 12 and 13 of the application as filed). Elaissari *et al.* neither teaches nor suggests that its polymeric species are suitable for implantation, let alone provide parameters and methods necessary for assessing such suitability. As such, the skilled practitioner would not be motivated to modify the teachings of Elaissari *et al.* to arrive at the instant invention. Accordingly, the instant claims are not obvious in view of this reference and Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 1-12 and 49 stand rejected under USC §103(a) as allegedly being unpatentable over Percot *et al.*, in view of Stile *et al.* (Macromolecules 1999, 32, 7370-7379). Percot *et al.* teaches hydrogels made of co-polymers of NiPAAm and N-ASI, while Stile *et al.* teaches hydrogels made of co-polymers of NiPAAm and AAc. The Examiner alleges that the combination of the Percot and Stile references possesses all of the claimed elements of the instant invention, thereby rendering the instant invention *prima facie* obvious. Applicants respectfully disagree, on the grounds that the instant species exhibit unexpected properties *vis a vis* the species allegedly taught or suggested by the combination of the Percot and Stile references. Specifically, the co-polymers of the instant invention possess a cloud point that is sufficiently low to ensure that a corneal implant or onlay that is prepared from said co-polymer will not become opaque (and therefore useless) under conditions in the human body or in test animals. The polymer matrix of the present invention is deliberately designed to have a lower critical solution temperature (LCST, *i.e.* "cloud point" or opacification point) which is well above physiological temperatures (*i.e.*, between about 35 °C and about 60 °C, or between about 42 °C and about 60 °C (see, *e.g.*, paragraph [0081] of the instant application as filed), ideally greater than 50 °C). See also, *e.g.*, Example 2 of the application as originally filed, wherein a

NiPAAM-co-AAc-co-ASI terpolymer solution remained clear up to 55 °C, consistent with a high LCST. By contrast, the Percot and Stile references teach co-polymers having LCST values that are well below physiological temperatures: Percot = 33.5-34.1°C (see, e.g., Table 1); Stile = 34.4+/-0.5°C (see, e.g., page 7374, right column, with NiPAAM-co-AAc). The co-polymers taught by the Percot and Stile references exhibit LCST values that are far too low for implantation in a patient (*i.e.*, they would lead to opaque, and therefore useless, implants). Therefore, one seeking to produce the hydrogel as presently claimed would not be motivated to consider the Percot or Stile references, alone or in combination. Thus, Applicants submit that the claims, as presently amended to recite a co-polymer which is suitable for implantation in a patient, are not obvious in view of the cited references. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claims 1-12 and 49 stand rejected under USC §103(a) as allegedly being unpatentable over Uludag *et al.*, in view of Stile *et al.* (Macromolecules 1999, 32, 7370-7379). Uludag *et al.* teaches hydrogels made of co-polymers of NiPAAm and N-ASI, while Stile *et al.* teaches hydrogels made of co-polymers of NiPAAm and AAc. The Examiner alleges that the combination of the Uludag and Stile references possesses all of the claimed elements of the instant invention, thereby rendering the instant invention *prima facie* obvious. Applicants respectfully disagree for the reasons set forth above, *i.e.*, the instant species exhibit unexpected properties *vis a vis* the species allegedly taught or suggested by the combination of the Uludag and Stile references. Specifically, the co-polymers of the instant invention possess a cloud point that is sufficiently low to ensure that a corneal implant or onlay that is prepared from said co-polymer will not become opaque (and therefore useless) under conditions in the human body or in test animals. The Uludag and Stile references teach co-polymers having LCST values that are well below physiological temperatures: Uludag = 28-31°C (referred to as CPT in Table I; also, on p. 589, Uludag states “we wanted to minimize any changes in the CPT of NASI-containing polymer from that of NiPAM homopolymer”); Stile = 34.4+/-0.5°C (see, e.g., page 7374, right column, with NiPAAM-co-AAc). Thus, the co-polymers taught by the Uludag and Stile references are unsuitable for implantation in a patient (*i.e.*, they would lead to opaque, and therefore, useless, implants). Therefore, one seeking to produce the hydrogel as presently claimed would not be motivated to consider the Uludag or Stile references, alone or in combination. Accordingly, Applicants submit that the claims, as presently amended to recite a

co-polymer which is suitable for implantation, are not obvious in view of the cited references. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

In view of the foregoing, entry of the amendments and remarks herein, reconsideration and withdrawal of all rejections, and allowance of the instant application with all pending claims are respectfully solicited. If there are any questions regarding the proposed amendments to the application, we invite the Examiner to call Applicants' representative at the telephone number below.

An extension of time and appropriate fee is being filed herewith. The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 12-0600, under Order No. OHR5-001US.

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Respectfully submitted,

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